I. Rejection of Claims 1-5, 7-14 and 16 Under 35 U.S.C § 112, First Paragraph

Claims 1-5, 7-14 and 16 stand rejected under 35 U.S.C § 112, second paragraph because the specification allegedly does not provide an enabling disclosure of the claimed invention.

This rejection is respectfully traversed as follows.

The specification teaches that administration of a demethylating agent or differentiating agent to cancerous thyroid cells results in activation of thyroid specific genes that had been transcriptionally inhibited. Several examples are provided wherein transcription of previously inhibited iodide transporter gene is restored in several different thyroid cancer cell lines, using several different demethylating or differentiating agents. In particular, it is demonstrated that iodide transport is restored by administering 5-azacytadine, a known demethylating agent. Thus, the specification provides an enabling disclosure of the invention as claimed.

Accordingly, the rejection of claims 1-5, 7-14 and 16 under 35 U.S.C § 112, first paragraph is respectfully traversed.

II. Rejection of Claim 16 Under 35 U.S.C § 112, First Paragraph

Claim 16 is rejected under 35 U.S.C § 112, first paragraph. The Examiner states that the specification fails to enable a method of restoring iodide transport to any dedifferentiated thyroid cancer cell by administering a demethylating agent to the cancerous cells.

Applicant respectfully disagrees with the Examiner's conclusion.

Applicant has demonstrated that administration of a demethylating agent to thyroid cancer cells encoding an iodide transporter gene that is transcriptionally inactivated due to hypermethylation results in demethylation and activation of the iodide transporter. Thus, one skilled in the art would not doubt that other demethylating agents can be used to demethylate hypermethylated iodide transporter genes to obtain re-activation of the gene.

Accordingly, the rejection of claim 16 under 35 U.S.C § 112, first paragraph is respectfully traversed.

III. Rejection of Claims 1-5, 7-14 and 16 Under 35 U.S.C § 112, First Paragraph

Claims 1-5, 7-14 and 16 stand rejected under 35 U.S.C § 112, first paragraph. The Examiner states that the claimed subject matter was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that the skilled practitioner would not be able to identify thyroid specific genes encoding therapeutic response elements and would not be able to identify the unblocking agents capable of inducing the re-expression of an inactivated response element gene, or of restoring sodium/iodide transport.

This rejection is respectfully traversed as follows.

It is respectfully submitted that one of skill in the art is capable of determining the thyroid specificity of a gene without undue experimentation and further, of identifying whether a thyroid specific gene encodes a therapeutic response element. Moreover, as

the examiner has noted, Applicants have provided multiple examples of unblocking agents that effectively activate the iodide transporter gene. Thus, the specification, combined with the level of skill in the at provides sufficient guidance to the skilled practitioner to practice the invention as claimed.

It is respectfully submitted that the rejection of claims 1-5, 7-14 and 16 under 35 U.S.C § 112, first paragraph is traversed.

IV. Rejection of Claims 1-5, 7-14 and 16 Under 35 U.S.C § 112, Second Paragraph

It is respectfully submitted that the rejection of claims 1-5, 7-14 and 16 under 35 U.S.C § 112, second paragraph is rendered moot by the amendments to the claims.

V. Rejection of Claims 1, 2, 4, 12, 13 and 15 Under 35 U.S.C § 102(b)

Claims 1, 2, 4, 12, 13 and 15 are rejected under 35 U.S.C § 102(b) as being unpatentably obvious over Schmutzler et al. The Examiner states that the cited reference discloses each and every element of the claims.

This rejection is respectfully traversed as follows.

As noted by the Examiner. Schmutzler et al. does not teach or suggest that iodide transport is restored by administration of retinoic acid to human thyroid carcinoma cell lines. Thus, the cited reference does not anticipate the claims as amended herein.

Accordingly, the rejection of claims 1-5, 7-14 and 16 under 35 U.S.C § 102(b) over Schmutzler et al. is respectfully taversed.

VI. Rejection of Claims 1, 2, 4, 12, 13, 15 and 16 Under 35 U.S.C § 102(b)

Claims 1, 2, 4, 12, 13, 15 and 16 are rejected under 35 U.S.C § 102(b) as being anticipated by Van Hearle. The Examiner state that the cited reference discloses each and every element of the claimed invention.

This rejection is respectfully traversed as follows.

In one aspect of the claimed invention there is provided a method for treating thyroid cancer cells which have lost the ability to transport iodine and which have an inactive thyroid specific response element. Applicants have shown that administration of a demethylating agent or differentiating agent other than retinoic acid to the cells results in expression of the therapeutic response element and uptake of iodine (claim 1). In this aspect of the invention, the therapeutic response element can be any protein or factor, such as an antigen, whose expression results in iodine uptake, either directly or indirectly.

In another aspect of the invention, there is provided a method of restoring iodine transport to dedifferentiated thyroid cancer cells in which the iodide symporter is inactive due to hypermethylation of the iodide symporter gene (claim 16). The method includes administration of a demethylating agent.

Van Hearle discloses administration of a differentiating agent (retinoic acid, which is not known as a demethylating agent) to thyroid cancer cells and a consequent increase in iodine transport in the treated cells. Thus, Van Hearle does not teach each and every aspect of amended claim 1. Furthermore, since Van Hearle does not teach administration of a demethylating agent, this reference does not anticipate claim 16.

Retinoic acid is not a demethylating agent and, although the administration of retinoic acid may indirectly result in iodine transport it does not achieve this effect by demethylation. As such, Van Hearle does not anticipate claim 16.

Accordingly, the rejection of claims 1, 2, 4, 13, 15 and 16 under 35 U.S.C § 102(b) over Van Hearle is respectfully traversed.

It is respectfully submitted that the present application, as amended, is in condition for allowance, an early notification thereof being earnestly solicited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such account.

Respectfully submitted,

MCDERMOTT, WILL & EMERY

Date: Oct. 1, 2002

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VERSION WITH MARKINGS SHOWING CHANGES MADE

IN THE CLAIMS:

Claim 1 (Twice Amended). A method of expressing a thyroid specific therapeutic response element in a human cancerous thyroid cell in which transcription of the gene encoding the response element and iodine transport into the cancerous cell was [blocked from expression] inhibited, comprising the step of administering an unblocking agent to the cancerous thyroid cell [harboring a gene encoding the response element], thereby resulting in the expression of the response element[,] and restoration of iodide transport into the cancerous cell, and wherein the unblocking agent is a demethylating or a differentiating agent other than retinoic acid.

Claim 16 (Twice Amended). A method of restoring iodide transport to dedifferentiated thyroid cancer cells comprising [the step of] administering a demethylating agent in an amount effective to transcriptionally activate a [thyroid specific therapeutic response element] hypermethylated sodium iodide symporter gene in [a] the thyroid cancer [cell] cells that [is] are defective in iodide transport, [wherein said thyroid specific therapeutic response element is a sodium iodide symporter], whereby iodine transport is restored to the dedifferentiated cancer cells.